250. *Studies in the Azole Series. Part VI. The Interaction of α-Amino-nitriles and* iso*Thiocyanates.*

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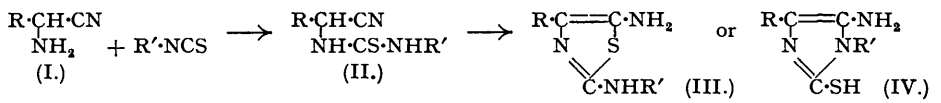
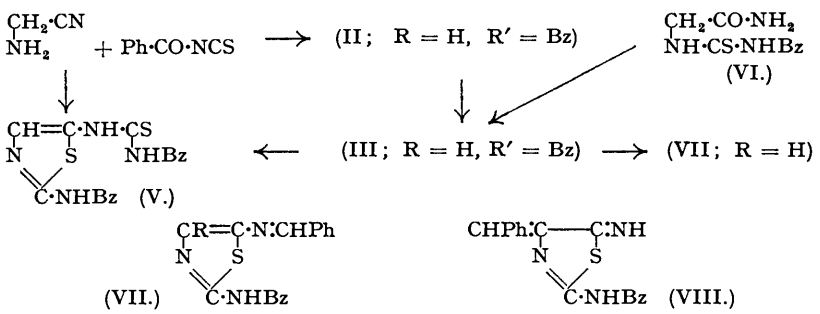
The interaction of aminoacetonitrile and benzoyl *iso*thiocyanate gives 5-amino- or 5-benzoylthioureido-2-benzamidothiazole according to conditions. The former rearranges under the influence of weak alkali into 5-benzamido-2-mercaptoglyoxaline, this isomerisation accounting for the varied products obtained on acetylation. Similarly, the use of α-aminobenzyl cyanide leads to 4-phenyl analogues of the above products. These results indicate that α-thioureido-nitriles such as (II; R = H, R′ = Bz) enjoy at most a transitory existence whereas corresponding ureas such as (XVI) show no tendency to undergo cyclisation.

Earlier parts of this series were concerned with the facile formation of 5-aminothiazoles where acyclic products might have been expected, and with the object of extending such syntheses. The present communication deals with the interaction of some α-amino-nitriles with *iso*thiocyanates, particularly benzoyl *iso*thiocyanate. This combination of reactants was selected as it presented the chance of obtaining either thiazoles or glyoxalines:



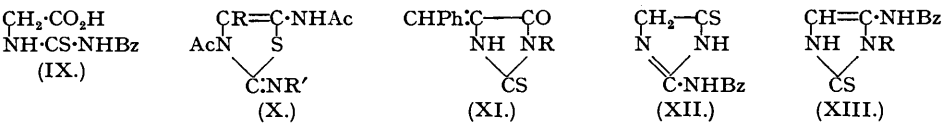
When benzoyl *iso*thiocyanate was allowed to react with aminoacetonitrile under mild conditions, combination took place between equimolecular quantities of the reactants with formation of a basic compound, $C_{10}H_9ON_3S$, giving a well-defined hydrochloride and *picrate*. On treatment of the base with nitrous acid it appeared to diazotise, giving a dark red dye on coupling with β-naphthol. For these and additional reasons appearing below the product was formulated as 5-*amino*-2-*benzamidothiazole* (III; R = H, R′ = Bz).



Convincing proof of the presence of a primary amino-group was provided by the formation of a Schiff's base, 2-*benzamido*-5-*benzylideneaminothiazole* (VII; R = H) with benzaldehyde. The remote possibility of this derivative being in fact a benzylidene derivative (VIII) of an imino-tautomeride of (III; R = H, R′ = Bz) was excluded by showing that substitution of the hydrogen atom in the 4-position in (III; R = H, R′ = Bz) in no way hindered condensation with benzaldehyde (see below). Again, the product (III; R = H, R′ = Bz) readily entered into further reaction with benzoyl *iso*thiocyanate to give a compound, $C_{18}H_{14}O_2N_4S_2$, which almost certainly is 2-*benzamido*-5-*benzoylthioureidothiazole* (V) (or a tautomeride thereof). The alternative thiourea (II; R = H, R′ = Bz) could hardly react in the above way, and indeed, it was shown that analogous substances failed to undergo any reaction with benzoyl *iso*thiocyanate under comparable conditions. Thus *N*-benzoyl-*N*′-methylthiourea was unaffected by benzoyl

*iso*thiocyanate, and incidentally by benzaldehyde also under the conditions used in forming the above Schiff's base. The compound (V) was also obtained directly from aminoacetonitrile sulphate in pyridine by reaction with benzoyl *iso*thiocyanate. In this connection N'-*benzoylthioureidoacetamide* (VI), prepared from aminoacetamide and benzoyl *iso*thiocyanate, was only weakly basic and underwent no further ready reaction with the latter reagent. Treatment with phosphorus tribromide, however, converted it into the *hydrobromide* of (III; R = H, R' = Bz) which also afforded the thioureido-derivative (V) by further reaction with benzoyl *iso*thiocyanate. Analogous was the conversion of the hydrochloride of (III; R = H, R' = Bz) into (V) by reaction with benzoyl *iso*thiocyanate.

The benzoyl group in (III; R = H, R' = Bz) was surprisingly firmly bound, vigorous acid hydrolysis of the compound bringing about ring-scission only with the formation of 2-thiohydantoin and *N*-benzoylthiohydantoic acid (IX) which was completely identified by its con-



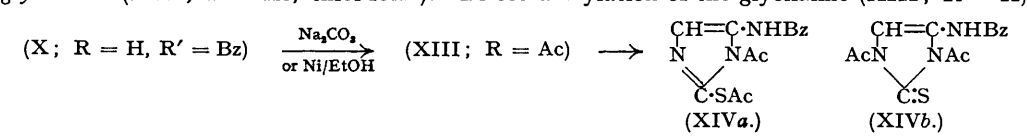
(IX.) (X.) (XI.) (XII.) (XIII.)

version into 3-benzoyl-5-benzylidene-2-thiohydantoin (XI; R = Bz) (Wheeler, Nicolet, and Johnson, *Amer. Chem. J.*, 1911, **46**, 468).

Whereas treatment of (III; R = H, R' = Bz) with benzoyl chloride gave 2 : 5-*dibenzamidothiazole*, acetylation gave more complex results. Excess of acetic anhydride gave a small yield of a diacetyl derivative, presumably (X; R = H, R' = Bz), together with a second product proved formally to be a monoacetyl derivative, though the following observations seem to establish that it was an acetyl derivative of a changed ring system.

The compound (III; R = H, R' = Bz) was devoid of pseudo-acidic properties, a fact clearly in keeping with its formulation and opposed to alternative cyclic structures such as (IV; R = H, R' = Bz). On being boiled with aqueous sodium carbonate, however, the thiazole (III; R = H, R' = Bz) was converted into a pseudo-acidic isomeride for which structures (IV; R = H, R' = Bz), (XII), and (XIII; R = H) came into consideration. The conversion of (III; R = H, R' = Bz) into (XII) would be entirely comparable with the isomerisation of 5-amino-2-mercaptothiazoles into dithiohydantoins (Parts II and III). On the other hand, the formation of (IV; R = H, R' = Bz) would represent an alternative still formally comparable with the known isomerisation mentioned above. Finally, the emergence of compound (XII; R = H) would represent simply a combination of the two changes already considered. Of these, the first can be excluded as the compound had no marked basic properties and failed to condense with benzaldehyde under conditions sufficing for the preparation of the Schiff's base (VII). Further, when treated with Raney nickel the new compound was very readily desulphurised, giving a substance which, though physically and chemically similar to 2-benzamidoglyoxaline (Fargher and Pyman, *J.*, 1919, **115**, 217), was not identical but isomeric with it. Structure (XII) is thus also excluded for the isomeride of 5-amino-2-benzamidothiazole and therefore the new compound must be 4(5)-*benzamido-2-mercaptoglyoxaline* (XIII; R = H), giving 4(5)-*benzamidoglyoxaline* by desulphurisation.

The above conclusion was supported by a further study of the results of acetylation of (III; R = H, R' = Bz). The diacetyl derivative (X; R = H, R' = Bz) was, as mentioned above, accompanied by a major quantity of a monoacetyl compound, $C_{12}H_{11}O_2N_3S$. The latter was also obtained by treating the diacetyl compound with sodium carbonate, and incidentally in abortive attempts to desulphurise it with Raney nickel in ethanol. Further acetylation of this monoacetyl derivative failed to regenerate the original diacetyl compound, an isomeric diacetyl derivative being obtained. It is probable therefore that the monoacetyl compound is not the thiazole but the acetyl derivative of (XIII; R = H). In view of its thiolic properties it is perhaps to be formulated as 4(5)-*benzamido-2-mercapto*-1- or -3-*acetylglyoxaline* (XIII; R = Ac, thiol form). Direct acetylation of the glyoxaline (XIII; R = H)



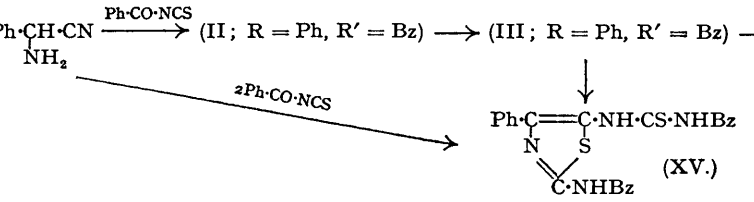
(X; R = H, R' = Bz) (XIII; R = Ac) (XIV*a*.) (XIV*b*.)

afforded a second monoacetyl derivative which, having regard to its origin and lack of pseudo-acidic properties, is tentatively regarded as 4(or 5)-*benzamido-2-acetylthioglyoxaline*, so that the

diacetyl compound mentioned above may be represented as 4(or 5)-*benzamido*-2-*acetylthio*-1- or -3-*acetylglyoxaline* (XIV*a*); it may be better represented by (XIV*b*), having regard to its inaccessibility from 4(or 5)-benzamido-2-acetylthioglyoxaline.

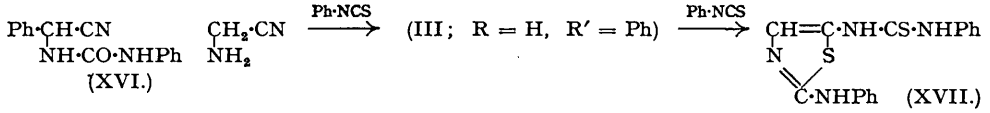
Finally, these considerations on the structure of compound (XIII) (and its derivatives) were confirmed by its hydrolysis to 2-thiohydantoin, identified as its 5-benzylidene derivative (XI; R = H) (Wheeler, Nicolet, and Johnson, *loc. cit.*).

Less extensive experiments employing α-aminobenzyl cyanide led to results which, as far as they were pursued, were very similar to those above. Reaction between equimolecular parts of the amino-nitrile and benzoyl *iso*thiocyanate in toluene led, not to the thiourea (II; R = Ph, R′ = Bz) which might have been expected, but to an isomeric base. The product is formulated as 5-*amino*-2-*benzamido*-4-*phenylthiazole* (III; R = Ph, R′ = Bz), for it was diazotisable and



afforded a *benzylidene* derivative (VII; R = Ph) as well as a *diacetyl* derivative, presumably (X; R = Ph, R′ = Bz). As with the analogous compound (III; R = H, R′ = Bz), the new thiazole (III; R = Ph, R′ = Bz) also reacted further with benzoyl *iso*thiocyanate, the product, 2-*benzamido*-5-*benzoylthioureido*-4-*phenylthiazole* (XV), being also obtainable directly from α-aminobenzyl cyanide.

The above facile cyclisations are, as expected, not observed in the corresponding oxygen series. For instance, ureidoacetonitrile, conveniently prepared from aminoacetonitrile and nitrourea (cf. Bailey, *Amer. Chem. J.*, 1897, **28**, 391), α-ureidobenzyl cyanide (Pinner and Lifschütz, *Ber.*, 1887, **20**, 2355; Pinner, *ibid.*, 1888, **21**, 2321), and α-*phenylureidobenzyl cyanide* (XVI) showed no tendency to pass into amino-oxazoles. On the other hand, aminoacetonitrile



and phenyl *iso*thiocyanate gave a very unstable base which combined with a second molecule of phenyl *iso*thiocyanate. On the basis of preceding reactions the last product is regarded as 2-*anilino*-5-*phenylureidothiazole* (XVII). Similarly, α-aminobenzyl cyanide and phenyl *iso*thiocyanate gave a stable base regarded as 5-*amino*-2-*anilino*-4-*phenylthiazole* (III; R = R′ = Ph) which formed a diacetyl derivative (X; R = R′ = Ph).

Experimental.

Lead thiocyanate (188 g.), benzoyl chloride (124 c.c.), and toluene (150 c.c.) were heated with stirring until reaction set in (*ca.* 80°), refluxed for 10 mins., and lead chloride separated from the cold solution and washed with toluene (30 c.c.). Fractionation of the solution in a vacuum gave benzoyl *iso*thiocyanate (104 g.), b. p. 135—138°/17 mm., which was redistilled and collected (yield, 93 g., 52%) at 95—97°/0·05 mm. (cf. Dixon, *J.*, 1899, **75**, 379; 1908, **93**, 692). The crude toluene solution could also be used for subsequent reactions.

Action of Benzoyl iso*Thiocyanate on Aminoacetonitrile.*—Benzoyl *iso*thiocyanate (12·2 c.c.) in ether (20 c.c.) was added during 15 mins. to aminoacetonitrile (Part III, this vol., p. 201) (5 g.) in ether (70 c.c.) with stirring at 0°. The oil solidified and after a further 10 mins. the colourless crystals (18 g.) were filtered off and washed with ether. 5-*Amino*-2-*benzamidothiazole* recrystallised from *ca.* 20 vols. of ethanol as colourless needles, m. p. 157° (decomp.) (yield, 13 g.) (Found : C, 54·8; H, 4·1; N, 18·8; S, 14·1. $C_{10}H_9ON_3S$ requires C, 54·8; H, 4·1; N, 19·2; S, 14·6%). Light absorption (chloroform) : $\lambda_{max.}$ = 2820 A., ϵ = 16,400; $\lambda_{inflex.}$ = 2400 A., ϵ = 21,900. Aminoacetonitrile (20 g.) was stirred with dry ether (200 c.c.) at 0°, and a crude toluene solution (140 c.c.) of benzoyl *iso*thiocyanate (≡ 58 g.) added during 20 mins. After a further 15 mins. the thiazole (63 g., 81%), identical with that above, was collected.

The *picrate* separated from ethanol in yellow needles, m. p. 163° (Found : C, 43·0; H, 2·8; N, 18·7; S, 7·2. $C_{16}H_{12}O_8N_6S$ requires C, 42·8; H, 2·7; N, 18·7; S, 7·2%). Stirring the thiazole (2 g.) with 4% ethanolic hydrogen chloride (35 c.c.) gave immediately the corresponding hydrochloride, m. p. 200—201° (decomp.), which was diazotised with sodium nitrite, and also gave 2-benzamido-5-benzoylthioureidothiazole under the same conditions as did the corresponding hydrobromide (see below).

The preceding thiazole (1·5 g.) in pyridine (20 c.c.) containing benzoyl *iso*thiocyanate (1 c.c.) was brought to boiling. On cooling and diluting with methanol (30 c.c.), 2-*benzamido-5-benzoylthioureidothiazole* (15 g.), m. p. 227°, separated. It separated from pyridine in lustrous green-yellow plates, m. p. 229° (decomp.) (Found: C, 56·4; H, 3·8; N, 14·8; S, 17·4. $C_{18}H_{14}O_2N_4S_2$ requires C, 56·5; H, 3·7; N, 14·7; S, 16·8%). Light absorption (in dioxan): $\lambda_{max.}$ = 2350, 2810, 3530 A., ϵ = 28,300, 29,800, 12,800, respectively; (in 0·1N-potassium hydroxide): $\lambda_{max.}$ = 2280 A., ϵ = 9550. This compound was also prepared as follows: Aminoacetonitrile sulphate (17 g.) was suspended in pyridine (60 c.c.), and a solution of benzoyl *iso*thiocyanate (27 g.) in toluene (200 c.c.) added while the mixture was stirred and slowly heated to boiling under reflux. An exothermic reaction set in and pyridine sulphate separated as a gum with some yellow crystals. Decanting and washing the deposit with ethanol (300 c.c.) removed the pyridine salt to leave the compound (5 g.) previously obtained, m. p. 228—229° (decomp.). 2-Benzamido-5-benzoylthioureidothiazole (1 g.) in 1N-sodium hydroxide (8 c.c.) was shaken with methyl sulphate. After 30 mins., dilution with water (15 c.c.) and neutralisation gave the *dimethyl* derivative (1 g.) as a yellow solid which after two recrystallisations from ethanol had m. p. 180° (decomp.) (Found: C, 58·6; H, 4·5; N, 13·4; S, 15·1. $C_{20}H_{18}O_2N_4S_2$ requires C, 58·5; H, 4·4; N, 13·7; S, 15·6%). Light absorption (chloroform): $\lambda_{max.}$ = 2490, 2810, 3340 A., ϵ = 25,400, 20,900, 22,150, respectively.

Aminoacetamide (10 g.) in ethanol (100 c.c.) and water (12 c.c.) was stirred at ~ 0° while benzoyl *iso*thiocyanate (18·3 c.c.) was added during 5 mins. After a further 15 mins. the solid (11 g.) was filtered off and dried. *N'-Benzoylthioureidoacetamide* recrystallised from ethanol in lustrous silky needles, m. p. 209—210° (slight decomp.) (Found: C, 50·9; H, 4·9; N, 17·6; S, 13·2. $C_{10}H_{11}O_2N_3S$ requires C, 50·6; H, 4·7; N, 17·7; S, 13·5%); light absorption (dioxan): $\lambda_{max.}$ = 2390, 2810 A., ϵ = 23,250, 9950. The preceding compound (3 g.) in hot dioxan (50 c.c.) was treated with phosphorus tribromide (0·5 c.c.). The copious cream precipitate (3·8 g.) was filtered off and washed with ether. *5-Amino-2-benzamidothiazole hydrobromide* had m. p. 198° (decomp.) and decomposed on attempted crystallisation (Found: N, 14·2. $C_{10}H_{10}ON_3SBr$ requires N, 14·0%). The hydrobromide gave a red solution with aqueous nitrous acid which afforded a deep red precipitate on addition to alkaline β-naphthol. The hydrobromide (1 g.) in pyridine (5 c.c.) was treated with benzoyl *iso*thiocyanate (0·5 c.c.) in pyridine (2 c.c.), and the mixture heated to boiling, cooled, and poured into methanol (25 c.c.). 2-Benzamido-5-benzoylthioureidothiazole (0·4 g.), m. p. and mixed m. p. with the material above 229°, was precipitated.

Miscellaneous Reactions of 5-Amino-2-Benzamidothiazole.—5-Amino-2-benzamidothiazole (5 g.) was refluxed with acetic anhydride (20 c.c.) for 15 mins. and the cold solution stirred into ice-water (250 c.c.) for 30 mins. The crude product (6·5 g., m. p. 124—127°) was crystallised repeatedly from ethanol to give *5-acetamido-2-benzimido-3-acetylthiazoline* as white lustrous plates, m. p. 185° (Found: C, 55·6; H, 4·4; N, 13·6; S, 10·4. $C_{14}H_{13}O_3N_3S$ requires C, 55·4; H, 4·3; N, 13·9; S, 10·6%). Light absorption (chloroform): $\lambda_{max.}$ = 2860 A., ϵ = 13,650; (0·01N-potassium hydroxide): $\lambda_{max.}$ = 2280, 3360 A., ϵ = 14,550, 14,550. The mother-liquors from the above diacetyl derivative were diluted with water, and the solid obtained crystallised repeatedly from methanol to give hydrated crystals of 4(5)-*benzamido-2-mercapto*-1- or 3-*acetylglyoxaline* (?) (1·7 g.) in colourless needles, m. p. 249—250°. When this was heated in a vacuum for 5 hours at 140°, the anhydrous substance was obtained as a white amorphous powder, m. p. 251° (Found: C, 55·0; H, 4·1; N, 15·8; S, 12·0. $C_{12}H_{11}O_2N_3S$ requires C, 55·1; H, 4·2; N, 16·1; S, 12·3%). Light absorption (ethanol): $\lambda_{max.}$ = 2290, 3150 A., ϵ = 13,050, 12,400; (0·1N-potassium hydroxide): $\lambda_{max.}$ = 2250, 3470 A., ϵ = 15,150, 12,800. The latter compound was also obtained by boiling the preceding diacetyl derivative (1·5 g.) with 10% aqueous sodium carbonate (20 c.c.) for 10 mins. and collecting the solid (1·35 g.). It was further obtained by boiling the same diacetyl derivative (1 g.) with Raney nickel (4—6 g.) in ethanol (20 c.c.).

4-Benzamido-2-mercapto-3-acetylglyoxaline (0·8 g.), refluxed with acetic anhydride (6 c.c.) for 10 mins., changed to a mass of green-yellow silky needles without melting. Pouring into water gave *4-benzamido-2-acetylthio-3-acetyliminazole* (?) (0·7 g.) which recrystallised from a large volume of acetic anhydride in needles, m. p. 199° (Found: C, 55·8; H, 4·5; N, 13·9; S, 10·1. $C_{14}H_{13}O_3N_3S$ requires C, 55·4; H, 4·3; N, 13·9; S, 10·6%). Light absorption (chloroform): $\lambda_{max.}$ = 3150 A., ϵ = 12,100; (in 0·1N-potassium hydroxide): $\lambda_{max.}$ = 2270, 3470 A., ϵ = 17,400, 14,550. The second acetyl group is very labile, crystallisation of the compound from pyridine giving almost entirely the original monoacetyl derivative.

5-Amino-2-benzamidothiazole (3 g.) was refluxed in benzene (50 c.c.) with benzoyl chloride (2 c.c.) for 90 mins. On cooling, the derivative (2·6 g.) was collected and recrystallised from nitrobenzene–ethanol, hydrated 2 : *5-dibenzamidothiazole* separating; m. p. 295° (decomp.) (Found, after drying at 56°: C, 59·5; H, 4·2; N, 12·1; S, 8·7. $C_{17}H_{15}O_3N_3S$ requires C, 59·8; H, 4·4; N, 12·3; S, 9·4%). Light absorption (ethanol): $\lambda_{max.}$ = 2280, 3240 A., ϵ = 22,850, 17,050. The monohydrate was dried in a vacuum at 140° to constant weight (54·9 Mg. lost 3·3 mg. of water. Calc. for 1 mol.: 3·15 mg.).

5-Amino-2-benzamidothiazole (2 g.) was refluxed with benzaldehyde (1 c.c.) in ethanol (40 c.c.) for 30 mins., the Schiff's base quickly separating. The *benzylidene* derivative (2·7 g.) crystallised from ethanol in yellow needles, m. p. 233° (Found: C, 66·7; H, 4·4; N, 13·5; S, 10·7. $C_{17}H_{13}ON_3S$ requires C, 66·4; H, 4·3; N, 13·7; S, 10·4%). Light absorption (chloroform): $\lambda_{max.}$ = 2350, 3050, 3660 A., ϵ = 23,000, 8000, 31,950, respectively.

5-Amino-2-benzamidothiazole (4 g.) was refluxed for 3 hrs. with ethanol (120 c.c.) while hydrogen chloride was passed in, then cooled and filtered; the filtrate was evaporated to dryness, and the residue taken up in water (30 c.c.) and neutralised with aqueous sodium carbonate. Ethyl ω-benzoylthiohydantoate was precipitated and recrystallised from ethanol in lustrous flakes, m. p. 130° (Wheeler, Nicolet, and Johnson, *loc. cit.*, quote m. p. 128—129°) (Found: S, 12·1. Calc. for $C_{12}H_{14}O_3N_2S$: S, 12·0%).

5-Amino-2-benzamidothiazole (5 g.) was refluxed for 40 mins. with concentrated hydrochloric acid (50 c.c.). The product was poured into ethanol (150 c.c.) and filtered hot. The solid, *N*-benzoylthiohydantoic acid, crystallised from dilute ethanol, had m. p. 199° (Wheeler, Nicolet, and Johnson give m. p. 202°). The preceding compound (0·25 g.), sodium acetate (0·3 g.), acetic acid (2·5 c.c.), acetic anhydride (1 c.c.), and benzaldehyde (0·25 c.c.) were heated together to 100—140° for 50 mins., and the

mixture poured into water (100 c.c.). The solid crystallised from ethanol as yellowish-red plates of 3-benzoyl-5-benzylidenethiohydantoin, m. p. 181° (lit., m. p. 181°). The filtrate from the above hydrolysis of 5-amino-2-benzamidothiazole on cooling gave 2-thiohydantoin, which separated from water in yellow crystals, m. p. 225—227° (decomp.) undepressed on mixing with an authentic specimen, m. p. 228° (decomp.). The benzylidene derivative of 2-thiohydantoin had m. p. 257—258°, also undepressed by authentic material, m. p. 258° (Wheeler, Nicolet, and Johnson, *loc. cit.*).

5-Amino-2-benzamidothiazole (5 g.) was refluxed for 5 mins. with 10% aqueous sodium carbonate (60 c.c.). On cooling, light brown crystals (4·3 g.) separated. 4(5)-*Benzamido-2-mercaptoglyoxaline* crystallised from ethanol in fine, colourless, hairy needles, decomposing at 240°, m. p. rather indefinite at 260° (Found: C, 54·5; H, 4·2; N, 19·5; S, 14·5. $C_{10}H_9ON_3S$ requires C, 54·8; H, 4·1; N, 19·2; S, 14·6%). Light absorption (ethanol): $\lambda_{max.}$ = 2670, 2280, 3050 A., ϵ = 17,100, 17,100, 6800, respectively. The compound coupled with sodium diazobenzene-*p*-sulphonate to give a carmine dye. On boiling the glyoxaline (1·5 g.) for 45 mins. with concentrated hydrochloric acid (10 c.c.) and then adding ethanol (25 c.c.), 2-thiohydantoin (0·5 g.) was precipitated. It crystallised from water in yellow needles, m. p. 226° (decomp.), identical with an authentic specimen. It was also identified as its benzylidene derivative, which crystallised from dilute acetic acid with m. p. 255—257° undepressed by the authentic material (Wheeler, Nicolet, and Johnson, *loc. cit.*).

4(or 5)-Benzamido-2-mercaptoglyoxaline (12 g.) was stirred in ethanol (400 c.c.) under reflux with Raney nickel (24 g.) for 1 hour. On filtration and concentration of the filtrate 4(or 5)-*benzamidoglyoxaline* (6 g.) separated in fine, colourless, hairy needles, m. p. 217° (slight decomp.), unchanged on recrystallisation from ethanol (Found: C, 64·2; H, 4·9; N, 22·3. $C_{10}H_9ON_3$ requires C, 64·1; H, 4·8; N, 22·5%). Light absorption (chloroform): $\lambda_{max.}$ = 2270 A., ϵ = 9350. A mixture with authentic 2-benzamidoiminazole gave m. p. *ca.* 200°.

4(5-)Benzamido-2-mercaptoglyoxaline (1 g.) was refluxed with acetic anhydride (10 c.c.) for 30 mins., and the cold solution poured into water (70 c.c.). The precipitate (0·6 g.) was recrystallised from ethanol to give 5-*benzamido-2-acetylthioiminazole* (?) as almost colourless needles, m. p. 204° (Found: C, 55·0; H, 4·3; S, 11·7. $C_{12}H_{11}O_2N_3S$ requires C, 55·1; H, 4·2; S, 12·3%).

Action of iso*Thiocyanates on α-Aminobenzyl Cyanide.*—A solution of α-aminobenzyl cyanide (15 g.) in toluene (230 c.c.) containing benzoyl *iso*thiocyanate (20 g.) was warmed slightly and then kept for 3 days. The yellow solid (22 g.) recrystallised from *n*-butanol to give 5-*amino-2-benzamido-4-phenylthiazole* as small, yellow, silky plates, m. p. 179° (Found: C, 65·4; H, 4·6; S, 10·5. $C_{16}H_{13}ON_3S$ requires C, 65·1; H, 4·4; S, 10·8%). Light absorption (in chloroform): $\lambda_{max.}$ = 3090 A., ϵ = 12,100; (in 0·1N-potassium hydroxide): $\lambda_{max.}$ = 2310, 3100 A., ϵ = 21,550, 4425. The compound was diazotised in acetic–sulphuric acid, the diazonium salt coupling with β-naphthol to give a red dye.

The preceding thiazole was boiled in pyridine with excess of benzoyl *iso*thiocyanate for 1 min., and the solution cooled and poured into ethanol. The product was 2-*benzamido-5-benzoylthioureido-4-phenylthiazole*, m. p. 203°, which was more conveniently prepared as follows: α-Aminobenzyl cyanide (5 g.) was kept overnight in ether (50 c.c.) with benzoyl *iso*thiocyanate (10 c.c.). The yellow deposit (6·7 g., m. p. 202°) crystallised from ethanol in pale yellow hairs of the monohydrate, m. p. 205° (Found: C, 60·3; H, 4·3; N, 11·9; S, 13·3. $C_{24}H_{20}O_3N_4S_2$ requires C, 60·5; H, 4·2; N, 11·8; S, 13·5%). Light absorption (in chloroform): $\lambda_{max.}$ = 2440, 2820, 3760 A., ϵ = 43,800, 26,200, 9,300, respectively; (in 0·1N-potassium hydroxide): $\lambda_{max.}$ = 3380 A., ϵ = 12,400. The monohydrate was dried in a vacuum at 140° to constant weight (47·8 Mg. lost 2·1 mg. Calc. for 1 mol.: 1·9 mg.).

5-Amino-2-benzamido-4-phenylthiazole (1 g.) was refluxed for 2 hrs. with acetic anhydride (10 c.c.), and the solution cooled and poured into ice-water (150 c.c.). Recrystallisation of the solid from ethanol gave 5-*acetamido-2-benzimido-3-acetyl-4-phenylthiazoline* (0·7 g.) as colourless needles, m. p. 180° (Found: C, 63·3; H, 4·8; N, 11·0; S, 8·7. $C_{20}H_{17}O_3N_3S$ requires C, 63·3; H, 4·5; N, 11·1; S, 8·5%). Light absorption (chloroform): $\lambda_{max.}$ = 2390, 2810, 2040 A., ϵ = 35,250, 17,450, 13,300, respectively.

5-Amino-2-benzamido-4-phenylthiazole (1·5 g.) was refluxed for 30 mins. in ethanol (30 c.c.) with benzaldehyde (0·5 c.c.), and the fine yellow needles (1·8 g.) collected. Recrystallisation from ethanol gave the *benzylidene* derivative as yellow needles, m. p. 197—198° (Found: C, 72·6; H, 4·7; N, 10·9. $C_{23}H_{17}ON_3S$ requires C, 72·1; H, 4·5; N, 11·0%). Light absorption (chloroform): $\lambda_{max.}$ = 2420, 2590, 3070, 3950 A., ϵ = 31,000, 31,000, 14,550, 25,650, respectively.

Phenyl *iso*cyanate (5·2 c.c.) was slowly added to α-aminobenzyl cyanide (5 g.) in ether (100 c.c.); heat was evolved and a bulky precipitate (7 g.) appeared. Recrystallisation from ethanol gave *α-phenylureidobenzyl cyanide* as white hairs, m. p. 155° (Found: C, 72·0; H, 5·2; N, 16·5. $C_{15}H_{13}ON_3$ requires C, 71·7; H, 5·2; N, 16·7%).

Nitrourea (10 g.), suspended in water (20 c.c.), was treated with aminoacetonitrile (5 g.) in water (10 c.c.). On warming the clear solution to 60—70° and allowing it to cool and the effervescence to subside, long needles of ureidoacetonitrile (6 g., m. p. 136—137°) separated; a further yield (2·7 g.) of slightly impure material was obtained from the mother-liquor. The urea, crystallised from ethanol, had m. p. 138° (Bailey, *Amer. Chem. J.*, 1897, **28**, 391, quotes m. p. 139°) (Found: N, 42·4. Calc. for $C_3H_5ON_3$: N, 42·4%) (cf. Davis, *J. Amer. Chem. Soc.*, 1929, **51**, 1790).

Phenyl *iso*thiocyanate (7 c.c.) was added to α-aminobenzyl cyanide (8 g.), and the mixture heated to boiling. After cooling, the crystalline solid was collected (3 g., m. p. 198—199°) and recrystallised from ethanol to give colourless needles of 5-*amino-2-anilino-4-phenylthiazole*, m. p. 199° (Found: C, 67·4; H, 4·9; N, 15·6; S, 12·4. $C_{15}H_{13}N_3S$ requires C, 67·4; H, 4·9; N, 15·7; S, 12·0%). Light absorption (ethanol): $\lambda_{max.}$ = 3130 A., ϵ = 15,100; (0·1N-potassium hydroxide): $\lambda_{max.}$ = 2290, 3080 A., ϵ = 18,700, 6250.

5-Amino-2-anilino-4-phenylthiazole (1 g.) was refluxed for 1 hour with acetic anhydride (10 c.c.), and the solution cooled and poured into water (50 c.c.). Recrystallisation of the solid from ethanol gave colourless needles of 5-*acetamido-2-phenylimino-3-acetyl-4-phenylthiazoline*, m. p. 245° (Found: C, 64·5; H, 5·0; N, 11·9; S, 9·2. $C_{19}H_{17}O_2N_3S$ requires C, 64·9; H, 4·9; N, 12·0; S, 9·1%). Light absorption (in chloroform): $\lambda_{max.}$ = 2950 A., ϵ = 18,250; (in 0·1N-potassium hydroxide): $\lambda_{inflex.}$ = 2900 A., ϵ = 11,600.

Phenyl *iso*thiocyanate (20 c.c.) in ether (25 c.c.) was slowly added to aminoacetonitrile (10 g.) with shaking. The solid (31·5 g.), m. p. 146—147°, presumably 5-amino-2-anilinothiazole, could not be crystallised satisfactorily. A portion (2·3 g.) was boiled in pyridine (5 c.c.) with phenyl *iso*thiocyanate (2 c.c.) for 1 min., and the solution poured into methanol (100 c.c.). The solid (2 g., m. p. 218—219°) was recrystallised from pyridine–ethanol, giving *2-anilino-5-phenylthioureidothiazole* as yellow microcrystals, m. p. 221° (Found: C, 58·4; H, 4·3; S, 19·8. $C_{16}H_{14}N_4S_2$ requires C, 58·8; H, 4·3; S, 19·7%). Light absorption (chloroform): $\lambda_{max.} = 3020, 3870$ A., $\epsilon = 12{,}050, 28{,}700$.

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